



UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office

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SERIAL NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.
07/010,085	04/11/84	TOOLE J	5031-A-PCT

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EXAMINER	
ESKIN, R	
ART UNIT	PAPER NUMBER
185	5

DATE MAILED:

03/22/89

This is a communication from the examiner in charge of your application.

COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☒ Responsive to communication filed on 12-27-88 ☒ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), _____ days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

- | | |
|--|---|
| 1. <input type="checkbox"/> Notice of References Cited by Examiner, PTO-892. | 2. <input type="checkbox"/> Notice re Patent Drawing, PTO-948. |
| 3. <input type="checkbox"/> Notice of Art Cited by Applicant, PTO-1449 | 4. <input type="checkbox"/> Notice of Informal Patent Application, Form PTO-152 |
| 5. <input type="checkbox"/> Information on How to Effect Drawing Changes, PTO-1474 | 6. <input type="checkbox"/> _____ |

Part II SUMMARY OF ACTION

1. ☒ Claims 1-31 are pending in the application.
Of the above, claims _____ are withdrawn from consideration.
2. ☒ Claims 1-19 have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☒ Claims 20-31 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings which are acceptable for examination purposes until such time as allowable subject matter is indicated.
8. ☐ Allowable subject matter having been indicated, formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. These drawings are ☐ acceptable; ☐ not acceptable (see explanation).
10. ☐ The ☐ proposed drawing correction and/or the ☐ proposed additional or substitute sheet(s) of drawings, filed on _____, has (have) been ☐ approved by the examiner. ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed _____, has been ☐ approved. ☐ disapproved (see explanation). However, the Patent and Trademark Office no longer makes drawing changes. It is now applicant's responsibility to ensure that the drawings are corrected. Corrections MUST be effected in accordance with the instructions set forth on the attached letter "INFORMATION ON HOW TO EFFECT DRAWING CHANGES", PTO-1474.
12. ☐ Acknowledgment is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received
☐ been filed in parent application, serial no. _____; filed on _____.
13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

Claim 29 is rejected under 35 U.S.C. 101 because as being directed to non-statutory subject matter.

The factor VIII :C protein in nature is proteolytically cleaved resulting in a functional polypeptide which comprises procoagulant activity. The resulting two-subunit protein comprises the same peptide structure as factor VIII :C, except for lacking the internal domain, is deemed to anticipate the instant protein as it is claimed in claim 29.

The following is a quotation of 35 U.S.C. 103 which forms the basis for all obviousness rejections set forth in this Office action:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

Claims 20-28 are rejected under 35 U.S.C. 103 as being unpatentable over Wood et al and Toole et al in view of Vehar et al.

The rejection is repeated for essentially the same reasons applied to claims 2-4 and 6-8 in the previous office action.

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Claims 29-31 are rejected under 35 U.S.C. 103 as being unpatentable over Toole et al and Wood et al in view of Vehar et al.

The rejection is repeated for essentially the same reasons applied to claim 13-15, 17-19 in the previous Office action.

Applicant's arguments are considered together as the issues appear to be the same.

Applicant argues that the deletion of the B domain would not have been obvious on three bases (1) it does not activate factor VIII :C (2) the internal domain may have had other functions required for factor VIII :C activation or processing and (3) that the resulting outcome , i.e substantially enhanced levels of factor VIII :C are unexpected.

In response to these points it is first noted that the claims are not limited to the DNA constructions which result in enhanced levels of factor VIII :C expression. All of the DNA claims encompass deletion of as few as one codon. It is hardly unexpected that the deletion of only one comdon from a DNA sequence which codes for a protein of 2351 amino acids results upon expression in a protein with procoagulant activity. It would seem more surprising if the reverse were true.

With respect to applicant's point that removal of the B domain by itself is not sufficient for activation

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(pointing to the fact that applicant's polypeptide is subject to thrombin activation, to essentially the same extent as native precursor factor VIII :C) this also is not surprising. The prior art, specifically Vehar et al, teaches that thrombin activation of the precursor single chain form of factor VIII :C result in removal of the B domain, followed by formation of a function two-subunit protein. Accordingly, applicant's polypeptide (as long as cleavage sites are preserved) would be subject to same activation process, resulting in the production of a functional two subunit protein.

With further respect to applicant's comments that factor VIII fragments of 90 and 80 Kd are not individually active, this is noted, but is also taught by the prior art. Vehar et al clearly teaches that the many similarities between factor V and factor VIII support conclusion that both are required for factor VIII activity.

With respect to applicant's comments that the internal region of factor VIII may be required for proper folding of the nascent polypeptide, or that glycosylation may be required for specific intracellular processing, it is noted that the claims only require deletion of a codon. It is not unexpected that this de minimus change does not adversely affect the processing of the protein into an active coagulant.

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With final respect to applicant's arguments concerning the "unexpected" levels of expression (pointing to the fact that factor V is similarly expressed at low levels and that it is of similar size with an internal glycosylated domain) it is reiterated that the claims are not limited to the DNA constructs which are expressed at the argued unexpected levels.

Accordingly, the unexpected results are not relevant as the claims are not limited to the factors which result in the enhanced levels of expression.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). The practice of automatically extending the shortened statutory period an additional month upon the filing of a timely first response to a final rejection has been discontinued by the Office. See 1021 TMOG 35.

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 CFR 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

Any inquiry concerning this communication should be directed to Examiner Teskin at telephone number 703-557-5996.

Teskin/kfo

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ROBIN TESKIN
EXAMINER
ART UNIT 185